(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The cefamandole sodium used in making the batch for cefamandole content, moisture, pH, and identity.

(*b*) The batch for cefamandole content, sterility, pyrogens, moisture, and pH.

(ii) Samples required:

(*a*) The cefamandole sodium used in making the batch: 10 packages, each containing approximately 500 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Cefamandole content.* Proceed as directed in §436.324 of this chapter, preparing the sample solution and calculating the cefamandole content as follows:

(i) *Sample solution.* Reconstitute the sample as directed in the labeling. If it is represented as a single-dose container, remove all the withdrawable contents with a suitable hypodermic needle and syringe. If the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Further dilute an aliquot of this solution with distilled water to obtain a concentration of 2.0 milligrams of cefamandole per milliliter (estimated). Transfer 5 milliliters of this solution to a 50-milliliter volumetric flask, add 30 milliliters of pH 2.3 buffer, dilute to volume with distilled water, and mix.

(ii) *Calculations.* Calculate the cefamandole content as follows:

$$\text{Milligrams of cefamandole} = \frac{A \times \text{Milligrams of working standard.} \times \text{Potency of working standard in micrograms per milligram} \times f}{B \times 50 \times 1{,}000}$$

where:

A=The peak height of the sample;

B=The peak height of the working standard;

f=The dilution factor of the sample.

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in §436.32(b) of this chapter, using a solution containing 50 milligrams of cefamandole per milliliter.

(4) [Reserved]

(5) *Moisture.* Proceed as directed in §436.201 of this chapter.

(6) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

[47 FR 20756, May 14, 1982, as amended at 50 FR 19919, May 13, 1985]

§442.211 Cefazolin sodium injectable dosage forms.

§442.211a Sterile cefazolin sodium.

The requirements for certification and the tests and methods of assay for sterile cefazolin sodium packaged for dispensing are described in §442.11a, except for the following additional requirements if it is packaged with lidocaine hydrochloride injection 0.5 percent U.S.P.:

(a) The pH, when reconstituted and diluted to 100 milligrams per milliliter with lidocaine hydrochloride injection 0.5 percent U.S.P., is not less than 5.5 and not more than 7.0.

(b) In addition to the information required by §442.11a (a)(3)(i), the following shall be submitted:

(1) The pH on the batch reconstituted with lidocaine hydrochloride injection 0.5 percent U.S.P.; and

(2) Results of tests and assays on the lidocaine hydrochloride injection 0.5 percent to show conformance with U.S.P. requirements.

[42 FR 18059, Apr. 5, 1977. Redesignated at 48 FR 33479, July 22, 1983]

§ 442.211b Cefazolin sodium injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefazolin sodium injection is a frozen aqueous solution of cefazolin sodium in an isoosmotic diluent. Each milliliter contains cefazolin sodium equivalent to either 10 milligrams or 20 milligrams of cefazolin per milliliter. Its cefazolin content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of cefazolin that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 4.5 and not more than 7.0. It passes the identity test. The cefazolin used conforms to the standards prescribed by § 442.10(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Requests of tests and assays on:

(a) The cefazolin used in making the batch for cefazolin content, moisture, heavy metals, and identity.

(b) The batch for cefazolin content, sterility, pyrogens, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(a) The cefazolin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Cefazolin content.* Proceed as directed in § 436.342 of this chapter, preparing the sample solution and calculating the cefazolin content as follows:

(i) *Preparation of sample solution.* Using a suitable hypodermic needle and syringe, transfer an accurately measured representative portion from each container, equivalent to 40 milligrams of cefazolin, to a 100-milliliter volumetric flask. Dilute to volume with buffer solution, pH 7.0, and mix. Transfer 10.0 milliliters of this solution to a 200-milliliter volumetric flask, add 5.0 milliliters of internal standard solution, dilute to volume with buffer solution, pH 7.0, and mix

(ii) *Calculation.* Calculate the milligrams of cefazolin per milliliter of sample as follows:

$$\text{Milligrams of cefazolin per milliliter} = \frac{R_u \times P_s \times d}{R_s \times 1{,}000}$$

where:

R_u=Area of the cefazolin peak in the chromatogram of the sample (at a retention time equal to that observed for the standard) /Area of internal standard peak;

R_s=Area of cefazolin peak in the chromatogram of the cefazolin working standard /Area of internal standard peak;

P_s=Cefazolin activity in the cefazolin working standard solution in micrograms per milliliter; and

d=Dilution factor of the sample.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, except inject a sufficient volume of the undiluted solution to deliver 50 milligrams of cefazolin per kilogram.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

(5) *Identity.* The high-pressure liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the cefazolin working standard.

[48 FR 33479, July 22, 1983; 48 FR 40516, Sept. 8, 1983; 49 FR 48184, Dec. 11, 1984, as amended at 55 FR 11583, Mar. 29, 1990]